BMC Cardiovascular Disorders

RESEARCH

Open Access

The multivariable prognostic models for severe complications after heart valve surgery

Yunqi Liu[1,2†], Jiefei Xiao[2,3†], Xiaoying Duan[6†], Xingwei Lu[4,5], Xin Gong[4,5], Jiantao Chen[1], Mai Xiong[1], Shengli Yin[1,2*], Xiaobo Guo[4,5*] and Zhongkai Wu[1,2*]

Abstract

Background: To provide multivariable prognostic models for severe complications prediction after heart valve surgery, including low cardiac output syndrome (LCOS), acute kidney injury requiring hemodialysis (AKI-rH) and multiple organ dysfunction syndrome (MODS).

Methods: We developed multivariate logistic regression models to predict severe complications after heart valve surgery using 930 patients collected retrospectively from the first affiliated hospital of Sun Yat-Sen University from January 2014 to December 2015. The validation was conducted using a retrospective dataset of 713 patients from the same hospital from January 2016 to March 2017. We considered two kinds of prognostic models: the PRF models which were built by using the preoperative risk factors only, and the PIRF models which were built by using both of the preoperative and intraoperative risk factors. The least absolute shrinkage selector operator was used for developing the models. We assessed and compared the discriminative abilities for both of the PRF and PIRF models via the receiver operating characteristic (ROC) curve.

Results: Compared with the PRF models, the PIRF modes selected additional intraoperative factors, such as auxiliary cardiopulmonary bypass time and combined tricuspid valve replacement. Area under the ROC curves (AUCs) of PRF models for predicting LCOS, AKI-rH and MODS are 0.565 (0.466, 0.664), 0.688 (0.62, 0.757) and 0.657 (0.563, 0.751), respectively. As a comparison, the AUCs of the PIRF models for predicting LOCS, AKI-rH and MODS are 0.821 (0.747, 0.896), 0.78 (0.717, 0.843) and 0.774 (0.7, 0.847), respectively.

Conclusions: Adding the intraoperative factors can increase the predictive power of the prognostic models for severe complications prediction after heart valve surgery.

Keywords: Multivariable prognostic model, Heart valve surgery, Low cardiac output syndrome, Acute kidney injury, Multiple organ dysfunction syndrome

Backgrounds

Heart valve disease (HVD) is a common cardiosurgery disease, mainly including rheumatic, degenerative, ischemic and myxoid valvular disease [1]. The 30-day mortality after heart valve surgery is about 4–6%, nearly two-fold higher than coronary artery bypass graft (CABG) [2–4]. The morbidity of HVD also increases with increasing aging population [5, 6].

*Correspondence: yshengl03@163.com; mc03gxb@126.com; wuzhk@mail.sysu.edu.cn
†Yunqi Liu, Jiefei Xiao and Xiaoying Duan have contributed equally to this work.
[1] Department of Cardiac Surgery, The First Affiliated Hospital of Sun Yat-Sen University, No.58, Zhongshan Road II, Guangzhou 510080, China
[4] Department of Statistical Science, School of Mathematics, Sun Yat-Sen University, Guangzhou, China
Full list of author information is available at the end of the article

In the past 30 years, there are numerous conventional prognostic models to predict in-hospital mortality for patients who underwent cardiac surgery, such as the European System for Cardiac Operation Risk Evaluation (EuroSCORE), Quality Measurement and Management Initiative (QMMI), Northern New England Cardiovascular Disease Study Group (NNECDSG), New York's Cardiac Surgery Reporting System (NYCSRE) and Society of Thoracic Surgeons (STS) score [3, 7–12]. However, these prognostic models mainly predict postoperative mortality for CABG by preoperative factors, neither heart valve surgery nor severe complications prediction is concerned.

As the clinical observations and researches show, the major causes of mortality were severe complications after heart valve surgery, such as low cardiac output syndrome (LCOS), acute kidney injury requiring hemodialysis (AKI-rH) and multiple organ dysfunction syndrome (MODS) [13–15]. These severe complications not only prolong hospital stay, but also increase the hospitalization expenses of patients. Meanwhile, some important intraoperative factors, especially cardiopulmonary bypass (CPB)-related factors significantly affect the complications and morbidity [16, 17].

Therefore, this study aims to provide a method considering both preoperative and intraoperative factors to predict severe complications for patients who underwent heart valve surgery within 30 days. Further, to provide a thought for these conventional prognostic models to more accurately predict mortality.

Methods

Patients selection

This was a retrospective observational study of total 1643 adult patients who underwent heart valve surgery from January 2014 to March 2017 in the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China. The 930 patients (445 males, 485 females) admitted from January 2014 to December 2015 were used for model development. The other 713 patients (370 males, 343 females) admitted from January 2016 to March 2017 were used for model validation.

The inclusion criteria for patients selection should be adult patients older than 18 years, without history of any mechanical assistant due to organ failure.

The investigation complied with the principles of the Declaration of Helsinki and was approved by the human ethics committee of the First Affiliated Hospital of Sun Yat-sen University. Written informed consent forms were obtained from all patients.

Data collection

The preoperative clinical data were collected from patients' demographics, medical histories, results of essential laboratory tests and routine imaging examinations. The intraoperative clinical data were collected from surgical approaches, defibrillation frequency, aortic occlusion time (AOT) and auxiliary CPB time (ACPBT). The postoperative clinical data were collected from severe complications, mechanical assistant and discharge status.

All patients had a 30-day follow-up after cardiac valve surgery. The endpoints were the postoperative severe complications (LCOS, AKI-rH and MODS) within 30 days. Treatment principles of patients with cardiac valve disease were coincidences with international guidelines [18–21].

The definitions of severe complications

LCOS: (1) cardiac index (CI) < 2 min m^2 and systolic blood pressure (SBP) < 90 mmHg; (2) mixed venous oxygen saturation (SvO_2) < 50% and arterial oxygen saturation (SaO_2) minus $SvO_2 \geq 30\%$; (3) metabolic acidosis: the base excess indicate (B.E.) < −4; (4) signs of tissue hypoperfusion; (5) the results of Swan-Ganz catheterization, pulse index contour cardiac output (PiCCO), and echocardiography [13, 22–25].

MODS: It's a frequent complication of systemic inflammatory response syndrome, which presences of altered organ function in an acutely ill patients such that homeostasis cannot be maintained without intervention [26].

AKI-rH: (1) blood creatinine (BCr) ≥ 3 times baseline or BCr ≥ 354 mmol/l with the elevated level ≥ 44 mmol/l within 48 h; (2) oliguria: urine output less than 0.3 ml/kg/h for ≥ 24 h; (3) anuria for ≥ 12 h [27–29].

Statistical analysis

Analyses were performed in R version 3.5.1.

Two variable selection methods were respectively applied to build prognostic models: (1) preoperative variables were selected to build preoperative risk factors (PRF) models; (2) both preoperative and intraoperative variables were selected to build preoperative and intraoperative risk factors (PIRF) models (Fig. 1).

Compared the two prognostic models, we could conclude whether the predictive power improved when intraoperative risk factors added. Besides, considered a significant correlation might exist between preoperative and intraoperative risk factors in PIRF models, synchronous variable selection was performed among all related preoperative and intraoperative risk factors, rather than selecting separately. Using the least absolute shrinkage selector operator (LASSO) or stepwise regression

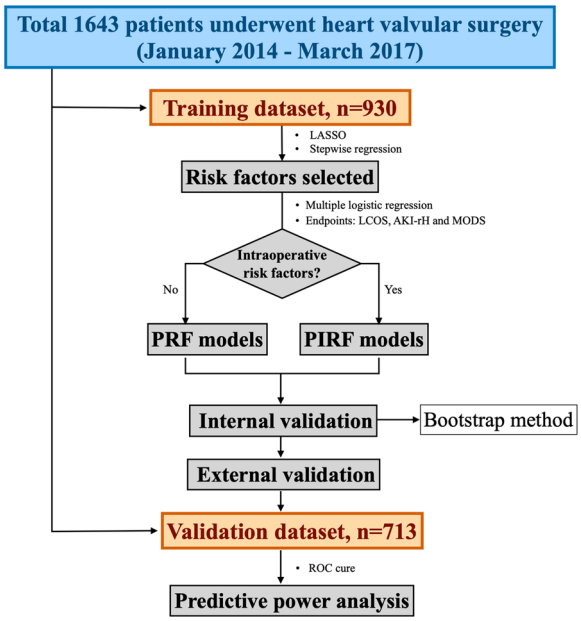

Fig. 1 Establishment and validation of PRF and PIRF models

analysis could effectively decrease the data dimensionality, further enhanced the predictive effect of the PIRF model. A multiple logistic regression was established to compare the selected risk factors between these two kinds of models which were respectively applied to predict the three endpoints (LCOS, AKI-rH and MODS).

During the evaluation period, internal and external validation were separately processed in these two kinds of models. In internal validation, bootstrap method with 1000 resampling was used to reduce overfitting of training dataset to obtain the internal evaluation results. In external validation, the prognostic models built by training dataset were applied for validation dataset to obtain the evaluation results. A multi-dimensional comparison included receiver operating characteristic curve (ROC) and the area under the ROC (AUC) of validation dataset was performed to estimate and compare the accuracy of PRF and PIRF models.

Results

Patients' characteristics

The characteristics of training and validation datasets are listed in Table 1. Compared the two datasets, the morbidities of severe complications are LCOS (9.46% vs. 5.33%, $P<0.05$), AKI-rH (4.48% vs. 7.29%, $P<0.05$) and MODS (4.95% vs. 4.49%, $P>0.05$), respectively.

The age in training dataset is younger than validation dataset (47.91 ± 13.83 vs. 49.68 ± 15 years, $P<0.05$). The morbidities of preoperative pulmonary disease (PD) and hepatitis of training dataset were higher than that of validation dataset (PD: 8.39% vs. 4.21%, $P<0.05$; hepatitis: 8.39% vs. 3.23%, $P<0.05$). More patients had a previous history of endocarditis in validation dataset than training dataset (16.83% vs. 9.46%, $P<0.05$). According to the results of echocardiography, preoperative eject functions (EF) of training and validation datasets are $62.71\pm10.14\%$ and $63.95\pm9.93\%$, respectively. Besides, pulmonary artery systolic pressure (PASP) in validation dataset is higher than that in training dataset (45.59 ± 17.4 mmHg vs. 21.86 ± 27.54 mmHg, $P<0.05$). Intraoperative AOT and ACPBT of training dataset are both shorter than those in validation dataset (AOT: 80.23 ± 34.7 min vs. 90.0 ± 46.7 min, $P<0.01$; ACPBT: 37.7 ± 22.5 min vs. 58.4 ± 40.2 min, $P<0.01$).

Prognostic models for LCOS

The PRF model for LCOS includes BCr (OR 1.85; 95% CI 0.95–3.59), creatinine clearance rate (CCr) (OR 0.46; 95% CI 0.32–0.67), hemoglobin (Hb) (OR 0.73; 95% CI 0.58–0.91), PAH (OR 1.34; 95% CI 0.96–1.86), and hypertension (OR 1.70; 95% CI 0.94–3.05) (Table 2). As a comparison, the PIRF model only includes CCr (OR 0.38; 95% CI 0.27–0.53) and ACPBT (OR 1.80; 95% CI 1.52–2.12). We applied both models to the validation dataset. The AUC of the PIRF model is 0.821 (0.747, 0.896), which is statistically higher ($P<0.01$) than that 0.565 obtained in the PRF model (Fig. 2, Table 5).

Prognostic models for AKI-rH

The PRF model for AKI-rH includes CCr (OR 0.33; 95% CI 0.21–0.52), red blood cell distribution width (RBC-DW) (OR 2.59; 95% CI 1.31–5.13) and total bilirubin (TBil) (OR 1.51; 95% CI 1.20–1.90) (Table 3). As a comparison, the PIRF model includes CCr (OR 0.36; 95% CI 0.22–0.57), RBC-DW (OR 2.19; 95% CI 1.08–4.43), TBil (OR 1.52; 95% CI 1.21–1.92) and ACPBT (OR 1.50; 95% CI 1.23–1.82). We applied both models to the validation dataset. The AUC of the PIRF model is 0.78 (0.717, 0.843), which is statistically higher ($P<0.01$) than that 0.688 obtained in the PRF model (Fig. 2, Table 5).

Prognostic models for MODS

The PRF model for MODS includes CCr (OR 0.28; 95% CI 0.18–0.45), BUN/BCr (OR 1.81; 95% CI 1.11–2.95), Hb (OR 0.74; 95% CI 0.55–1.01), heart failure history (OR 1.84; 95% CI 0.82–4.16) and PD (OR 3.33; 95% CI 1.55–7.16) (Table 4). As a comparison, the PIRF model includes CCr (OR 0.29; 95% CI 0.17–0.48), BUN/BCr (OR 1.86; 95% CI 1.1–3.14), CF (< 4 weeks) (OR 1.95; 95% CI 0.83–4.58), PD (OR 4.69; 95% CI 2.10–10.47), ACPBT (OR 1.71; 95% CI 1.41–2.09) and combined with tricuspid valve replacement (cTVR) (OR 3.69; 95% CI 1.16–11.47). We applied both models to

Table 1 Patient characteristics

Characteristics	Training dataset (n = 930)	Validation dataset (n = 713)	*P*
Demographics			
Age (y)	47.91 ± 13.83	49.68 ± 15.00	0.001
Gender (female, No. %)	485(52.15%)	343(48.11%)	0.115
Height (cm)	160.73 ± 8.18	160.49 ± 10.69	0.939
Weight (kg)	54.66 ± 10.39	56.96 ± 11.95	< 0.01
BMI	21.08 ± 3.29	21.97 ± 3.62	< 0.01
BSA (m^2)	6.87 ± 1.29	7.15 ± 1.49	< 0.01
Smoke (No. %)	166 (17.85%)	95(13.32%)	0.016
Medical histories			
CF (< 4 weeks, No. %)	601(64.62%)	421(59.05%)	0.024
Endocarditis (No. %)	88(9.46%)	120(16.83%)	< 0.01
Diabetes (No. %)	48(5.16%)	49(6.87%)	0.176
Hypertension (No. %)	122(13.12%)	129(18.09%)	0.007
Hepatitis (No. %)	78(8.39%)	23(3.23%)	< 0.01
Pulmonary disease (No. %)	78(8.39%)	30(4.21%)	0.001
Dialysis (No. %)	0(0.00%)	0(0.00%)	< 0.01
PVD (No. %)	0(0.00%)	0(0.00%)	< 0.01
Re-operation (No. %)	58(6.24%)	52(7.29%)	0.453
Laboratory values			
WBC ($\times 10^9$/l)	7.04 ± 2.46	7.22 ± 2.38	0.076
PLT ($\times 10^{12}$/l)	213.26 ± 66.44	217.74 ± 82.53	0.789
RBC ($\times 10^9$/l)	4.68 ± 0.70	4.58 ± 0.76	0.003
RBC-DW	0.14 ± 0.02	0.14 ± 0.03	< 0.001
< 0.12	3(0.32%)	1(0.14%)	
0.12–0.15	772(83.01%)	560(78.54%)	
> 0.15	148(15.91%)	151(21.18%)	
Hb (g/l)	133.78 ± 19.63	130.54 ± 21.53	0.001
ALT (u/l)	25.79 ± 33.6	26.94 ± 29.51	0.998
ALB (g/l)	42.29 ± 18.01	39.36 ± 4.92	< 0.01
TBil (mmol/l)	15.88 ± 10.39	16.52 ± 9.76	0.001
BUA (mg/l)	374.78 ± 122.51	423.22 ± 140.87	< 0.01
BUN (mmol/l)	6.12 ± 2.51	6.15 ± 2.93	0.249
< 2.9	24(2.58%)	22(3.09%)	
2.9–8.6	802(86.24%)	606(84.99%)	
> 8.6	95(10.22%)	84(11.78%)	
BCr (umol/l)	77.19 ± 27.07	86.11 ± 68.24	0.01
< 50	56(6.02%)	43(6.03%)	
50–115	808(86.88%)	609(85.41%)	
116–200	55(5.91%)	51(7.15%)	
> 200	3(0.32%)	9(1.26%)	
BUN/BCr	0.08 ± 0.04	0.08 ± 0.03	< 0.01
< 0.055 (No. %)	127(13.66%)	143(20.06%)	
0.055–0.075 (No. %)	308(33.12%)	250(35.06%)	
> 0.075 (No. %)	486(52.26%)	319(44.74%)	
CCr (ml/min/1.73m^2, No.)	79.62 ± 34.28	76.17 ± 26.37	0.046
< 50 (No. %)	116(12.47%)	98(13.74%)	
50–80 (No. %)	396(42.58%)	338(47.41%)	
> 80 (No. %)	404(43.44%)	275(38.57%)	

Table 1 (continued)

Characteristics	Training dataset (n = 930)	Validation dataset (n = 713)	*P*
APTT (secs.)	29.3 ± 5.72	31.74 ± 6.75	< 0.01
Fbg (g/l)	3.08 ± 1.16	3.08 ± 1.20	0.419
ESR (mm)	23.49 ± 20.45	26.16 ± 23.34	0.192
ECG measurements			
Atrial fibrillation (No. %)	389(41.83%)	235(32.96%)	< 0.01
UCG measurements			
LVD (mm)	54.51 ± 11.10	53.65 ± 10.97	0.220
EF (%)	62.71 ± 10.14	63.95 ± 9.93	0.005
> 50	777(83.55%)	612(85.83%)	
30–50	93(10%)	72(10.1%)	
< 30	4(0.43%)	1(0.14%)	
PASP (mmHg)	21.86 ± 27.54	45.59 ± 17.4	< 0.01
> 60	80(8.6%)	86(12.06%)	
30–60	310(33.33%)	380(53.3%)	
< 30	540(58.06%)	57(7.99%)	
Intraoperative variables			
AOT (min)	80.23 ± 34.70	90.0 ± 46.70	0.001
ACPBT (min)	37.7 ± 22.50	58.4 ± 40.20	< 0.01
Defibrillation (freq.)			0.351
< 1	773(83.12%)	605(84.85%)	
≥ 1	157(16.88%)	108(14.79%)	
Surgical approaches			
AVR (No. %)	378(40.65%)	293(41.09%)	0.894
MVR (No. %)	684(73.55%)	432(60.59%)	< 0.01
TVR (No. %)	33(3.55%)	31(4.35%)	0.483
MVP (No. %)	57(6.13%)	84(11.78%)	< 0.001
TVP (No. %)	298(32.04%)	303(42.5%)	< 0.001
CABG (No. %)	28(3.01%)	32(4.49%)	0.147
RFA (No. %)	27(2.9%)	33(4.63%)	0.086
Other cardiac surgery (No. %)	60(6.45%)	210(29.45%)	< 0.001
Non-cardiac surgery (No. %)	4(0.43%)	0(0.00%)	0.138
Severe complications			
LCOS (No. %)	88(9.46%)	38(5.33%)	0.002
AKI-rH (No. %)	45(4.84%)	52(7.29%)	0.047
MODS (No. %)	46(4.95%)	32(4.49%)	0.752
Mechanical assistant			
IABP /ECMO (No. %)	33(3.55%)	29(4.07%)	0.677
Discharge status			
Death (No. %)	61(6.56%)	47(6.59%)	1.000

the validation dataset. The AUC of the PIRF model is 0.774 (0.70, 0.847), which is statistically higher ($P < 0.01$) than that 0.657 obtained in the PRF model (Fig. 2, Table 5).

Discussions

The postoperative mortality of cardiac surgery obviously declines to 1–2%, but the morbidity of postoperative severe complications (LCOS, AKI-rH and MODS) still remains high, caused by surgical trauma, CPB-related injury, ischemia–reperfusion, endotoxemia, and blood transfusion repeatedly [24, 30]. These complications will

Table 2 Prognostic models for LCOS in development dataset

Variables	PRF model (n = 930)			PIRF model (n = 930)		
	β	OR (95% CI)	*P*	β	OR (95% CI)	*P*
Intercept	− 2.4909	0.08	0.015	− 0.3645	0.69	0.311
BCr	0.6152	1.85 (0.95–3.59)	0.068			
CCr	− 0.7756	0.46 (0.32–0.67)	< 0.01	− 0.9801	0.38 (0.27–0.53)	< 0.01
Hb	− 0.3191	0.73 (0.58–0.91)	0.006			
PASP	0.2929	1.34 (0.96–1.86)	0.082			
Hypertension	0.5281	1.70 (0.94–3.05)	0.079			
ACPBT				0.5855	1.80 (1.52–2.12)	< 0.01

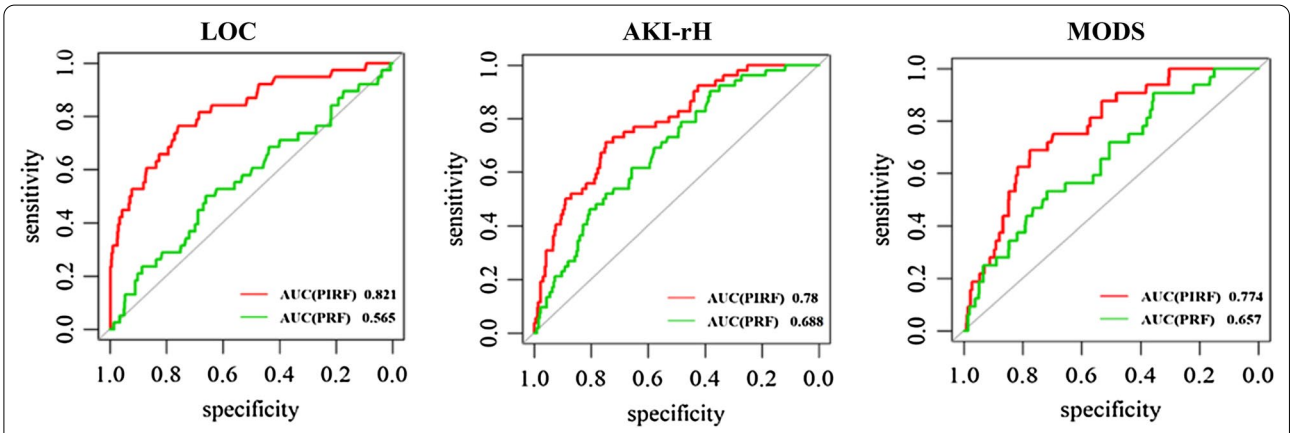

Fig. 2 ROC curve for different complications in validation datasets

Table 3 Prognostic models for AKI-rH in development dataset

Variables	PRF model (n = 930)			PIRF model (n = 930)		
	β	OR (95%CI)	*P*	β	OR (95% CI)	*P*
Intercept	− 2.9392	0.05	0.002	− 2.8605	0.06	0.004
CCr	− 1.1041	0.33 (0.21–0.52)	< 0.01	− 1.0247	0.36 (0.22–0.57)	< 0.01
RBC-DW	0.9530	2.59 (1.31–5.13)	0.006	0.7835	2.19 (1.08–4.43)	0.030
TBil	0.4093	1.51 (1.20–1.90)	0.001	0.4206	1.52 (1.21–1.92)	< 0.01
ACPBT				0.4042	1.50 (1.23–1.82)	< 0.01

prolong hospital stay and increase hospitalization costs [31, 32] .

Postoperative LCOS is one of the most serious complications and major cause to high mortality [13]. Around 70% of postoperative cardiac surgery patients have signs of ventricular systolic and diastolic dysfunction. Brain, liver, and kidney failure are common consequences of LCOS, eventually leading to MODS. In this study, we re-selected and re-determined relative risk variables by adding intraoperative factors and found that only CCr and ACPBT were the independent risk factors for postoperative LCOS. Manjula et al. also suggested preoperative renal failure (OR 4.9) was the most influential predictor for postoperative LCOS in the isolated aortic valve surgery [33]. Auxiliary cardiopulmonary bypass is a important way to repay myocardial ischemic oxygen debt with total bypass [34, 35]. But the clear advice on what is the optimal ACPBT is still not available from the

Table 4 Prognostic models for MODS in development dataset

Variables	PRF model (n = 930)			PIRF model (n = 930)		
	β	OR (95% CI)	*P*	β	OR (95% CI)	*P*
	− 2.5690	0.08	0.002	− 3.0533	0.05	0.001
CCr	− 1.2645	0.28 (0.18–0.45)	< 0.01	− 1.2457	0.29 (0.17–0.48)	< 0.01
BUN/BCr	0.5907	1.81 (1.11–2.95)	0.018	0.6219	1.86 (1.10–3.14)	0.020
Hb	− 0.296	0.74 (0.55–1.01)	0.057			
CF	0.6110	1.84 (0.82–4.16)	0.141	0.6660	1.95 (0.83–4.58)	0.127
PD	1.2038	3.33 (1.55–7.16)	0.002	1.5459	4.69 (2.10–10.47)	< 0.01
ACPBT				0.5381	1.71 (1.41–2.09)	< 0.01
cTVR				1.3049	3.69 (1.16–11.47)	0.027

Table 5 Comparisons of PRF and PIRF models for three complications in validation dataset

Complications	AUC		
	PRF model (n = 713)	PIRF model (n = 713)	*P*
LCOS	0.565 (0.466, 0.664)	0.821 (0.747, 0.896)	< 0.01
AKI-rH	0.688 (0.62, 0.757)	0.78 (0.717, 0.843)	< 0.01
MODS	0.657 (0.563, 0.751)	0.774 (0.7, 0.847)	0.003

scientific literature [36, 37]. ACPBT is often empirically controlled at the 20–30% of AOT, prolonged ACPBT could also decrease the difficulty of weaning from CPB [38, 39].

Postoperative AKI-rH is another cause to high mortality. More than 35% of patients before heart valve surgery have a previous history of chronic kidney disease, it is also a significant independent predictor of postoperative short-and long-term mortality [14, 40]. Approximately 40–50% of patients underwent heart valve surgery have acute kidney injury (AKI) attributed to ischemia–reperfusion injury during surgery, especially for the elder, diabetic and coronary artery disease (CAD) patients [40, 41]. The incidence of AKI-rH is nearly 1–3%, it is on the rise due to the increase of surgery complexity and tends to cause end-stage renal disease (ESRD) [4, 29, 42]. Compared the risk factors for postoperative AKI-rH between PRF and PIRF model, we found ACPBT was added additionally in the PIRF model besides the perioperative CCr, RBC-DW and TBil, it also proved that intraoperative factors could affect the patients' prognosis. High-preoperative RBC-DW could result from the decrease in erythropoietin (EPO) production and chronic heart failure, increasing the in-hospital mortality with AKI after cardiac surgery [43–45]. Elisabeth et al. also showed the high TBil level is prone to develop cholemic nephropathy, due to impair the structure of tubular epithelial plasma membranes and mitochondria [46, 47].

Postoperative MODS is a common final cause to death in critically ill patients, the mortality is approximately 54% [15, 31, 48, 49]. In most cases, patients with MODS are supported by continuous vasoactive agents or mechanism assistances to maintain vital signs [50]. The nature of MODS focuses on the crosstalk among different organs, damage from one organ could induce secondary injury for another organ, finally active a vicious circle [51]. Higher than 5% of postoperative patients will develop to MODS, especially LCOS and AKI-rH are combined [52]. In Table 4, intraoperative risk factors including ACPBT and cTVR were new predictors for postoperative MODS besides CCr, BUN/BCr and PD, we also found PD (OR 4.69) and cTVR (OR 3.69) were the high-risk factors for postoperative MODS. Researchers showed surgical intervention for severe tricuspid valve disease is only indicated in symptomatic patients, or who have severe comorbidities [53, 54]. Sharma et al. reported that right ventricular failure is related to nearly 40% kidney failure and has an increased mortality risk after TVR [55].

Currently, there are two classical prognostic models to predict in-hospital morality after heart valve surgery, the Society for Thoracic Surgeons (STS) score (https://www.sts.org/resources/risk-calculator) and European System for Cardiac Operative Risk Evaluation (EuroSCORE) II (http://www.euroscore.org/calc.html) [56, 57]. The limitations for these models were found as follows: the major endpoint is mortality, predictive accuracy only relies on preoperative factors, and model-based design of patients underwent CABG instead of heart valve surgery. Postoperative renal failure is the only common endpoint for STS score and PIRF model. The AUC of renal failure in the PIRF model is very close to that in STS score (0.780 vs. 0.787). But the PIRF model is a more simplified model

with only 4 independent variables. Besides, the postoperative morbidity was defined quite differently by STS score and our PIRF model, the definition proposed by STS score applied to a wider range than PIRF model. Although a direct comparison between STS score and PIRF model could not be made, according to the official website of STS 2018 score, we find the AUC of postoperative morbidity in the STS score is lower than that in our PIRF model (STS score: 0.723 vs. PIRF model: LCOS 0.821, AKI-rH 0.780, MODS 0.774).

Basing on clinical observations and recent research results, important intraoperative factors can influence the prognosis of patients and the postoperative severe complications are associated with increased mortality. Nearly all variables contained in both STS score and EuroSCORE II are adopted in this study, besides, addition of the new variables of intraoperative risk factors were added. The endpoints in our study include postoperative sever complications, but not mortality. We proved that the intraoperative risk factors, especially ACPBT was the common independent risk factor for all endpoints (LCOS: OR 1.80; AKI-rH: OR 1.50; MODS: OR 1.71). Therefore, we provided a method for predicting severe complications morbidities after heart valve surgery by both preoperative and intraoperative factors are considered. Besides, the predictive power of PIRF models is more accurate and reliable compared with PRF models. Basing on this study, we provided a thought for conventional model to improve the predictive power for mortality and adjust treatment planning in time.

As a retrospective study, it also has some limitations. The sample size is limited by a single-center research and only focus on postoperative complications within 30 days. Therefore, it is necessary to validate the multivariable prognostic model by using a larger sample size from multiple centers and focus on long-term prognosis in the future.

Conclusions

In this study, we consider both preoperative and intraoperative factors to predict severe complications morbidities after heart valve surgery, providing a further thought to improve the predictive power of conventional prognostic model for patients underwent heart valve surgery. After re-selected and re-determined relative risk variables, the PIRF model was more accurate and reliable by adding the intraoperative factors, which will help us adjust treatment planning in time to decrease mortality eventually.

Abbreviations

ACPBT: Auxiliary cardiopulmonary bypass time; AKI: Acute kidney injury; AKI-rH: Acute kidney injury requiring hemodialysis; ALB: Albumin; ALT: Alanine transaminase; AOT: Aortic occlusion time; APTT: Activated partial thromboplastin time; AUC: The area under the receiver-operator characteristic (ROC) curve; AVR: Aortic valve replacement; BCr: Blood creatinine; B.E.: Base excess indicate; BMI: Body mass index; BSA: Body surface area; BUA: Blood uric acid; BUN: Blood urea nitrogen; BUN/BCr: Blood urea nitrogen/blood creatinine; CABG: Coronary artery bypass graft surgery; CAD: Coronary artery disease; CAG: Coronary angiography; CCr: Creatinine clearance; CI: Cardiac index; CPB: Cardiaopulmonary bypass; CPBT: CPB time; cTVR: Combined tricuspid valve replacement; ECG: Electrocardiogram; ECMO: Extracorporeal membrane oxygenation; EF: Ejection fraction; ESR: Erythrocyte sedimentation rate; ESRD: End-stage renal disease; EuroSCORE: European system for cardiac operation risk evaluation; Fbg: Fibrinogen; GFR: Glomerular filtration rate; Hb: Hemoglobin; CF: Cardiac failure; HVD: Heart valve disease; IABP: Intra-aortic balloon pump; ICU: Intensive care unit; LASSO: Least absolute shrinkage selector operator; LCOS: Low cardiac output syndrome; LVD: Left ventricular dimension; MODS: Multiple organ dysfunction syndrome; MVP: Mitral valvuloplasty; MVR: Mitral valve replacement; NNECDSG: Northern New England cardiovascular disease study group; NYCSRE: New York's cardiac surgery reporting system; PASP: Pulmonary artery systolic pressure; PiCCO: Pulse index contour cardiac output; PLT: Platelet; PIRF: Preoperative and intraoperative risk factors; PRF: Preoperative risk factors; PVD: Peripheral vascular disease; QMMI: Quality measurement and management initiative; RFA: Radiofrequency ablation; RBC: Red blood cell; RBC-DW: Red blood cell distribution width; ROC: Receiver operating characteristic curve; SaO_2: Arterial oxygen saturation; STS: Society of thoracic surgeons; SvO_2: Mixed venous oxygen saturation; TBil: Total bilirubin; TVP: Tricuspid valvuloplasty; TVR: Tricuspid valve replacement; UCG: Ultrasound cardiography; WBC: White blood cell.

Acknowledgements

Not applicable.

Authors' contributions

YL designed this retrospective research and interpreted patient's clinical data; JX and XD wrote the manuscript; XL performed statistical analysis of the data set; XG verified the data set; JC collected and recorded the patient's clinical data; MX amended the manuscript; ZW, SY performed the surgical treatment; XG was responsible for the design and quality control of the statistical program; ZW supervised the research and was responsible for the overall research quality control. All authors read and approved the final manuscript.

Funding

This work was supported by the National Natural Science Foundation of China (NSFC) (11771463), Pearl River S&T Nova Program (201806010142) and Science and Technology Planning Project of Guangdong Province (2015B010125001 and 201803010077).

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

All the protocols in this study were approved by the human ethics committee of the First Affiliated Hospital of Sun Yat-sen University and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent forms were obtained from all patients.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details
[1]Department of Cardiac Surgery, The First Affiliated Hospital of Sun Yat-Sen University, No.58, Zhongshan Road II, Guangzhou 510080, China. [2]NCH Key Laboratory of Assisted Circulation, Sun Yat-Sen University, Guangzhou 510080, China. [3]Department of Extracorporeal Circulation, The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510080, Guangdong, China. [4]Department of Statistical Science, School of Mathematics, Sun Yat-Sen University, Guangzhou, China. [5]Southern China Center for Statistical Science, Sun Yat-Sen University, Guangzhou 510275, China. [6]Department of Emergency, the Eighth Affiliated Hospital of Sun Yat-sen University, Shenzhen 518000, China.

Received: 21 April 2021 Accepted: 11 September 2021
Published online: 11 October 2021

References

1. Coffey S, Cairns BJ, Iung B. The modern epidemiology of heart valve disease. Heart. 2016;102(1):75–85.
2. Lee R, Li S, Rankin JS, O'Brien SM, Gammie JS, Peterson ED, McCarthy PM, Edwards FH. Fifteen-year outcome trends for valve surgery in North America. Ann Thorac Surg. 2011;91(3):677–84 (**discussion p 684**).
3. Hansen LS, Hjortdal VE, Andreasen JJ, Mortensen PE, Jakobsen CJ. 30-day mortality after coronary artery bypass grafting and valve surgery has greatly improved over the last decade, but the 1-year mortality remains constant. Ann Card Anaesth. 2015;18(2):138–42.
4. Nadim MK, Forni LG, Bihorac A, Hobson C, Koyner JL, Shaw A, Arnaoutakis GJ, Ding X, Engelman DT, Gasparovic H, et al. Cardiac and vascular surgery-associated acute kidney injury: the 20th international consensus conference of the ADQI (Acute Disease Quality Initiative) group. J Am Heart Assoc. 2018;7(11):e008834.
5. Kodali SK, Velagapudi P, Hahn RT, Abbott D, Leon MB. Valvular heart disease in patients ≥80 years of age. J Am Coll Cardiol. 2018;71(18):2058–72.
6. Gaede L, Aarberge L, Brandon Bravo Bruinsma G, Macarthy P, Musumeci F, Zamorano P, Möllmann H. Heart valve disease awareness survey 2017: what did we achieve since 2015? Clin Res Cardiol. 2019;108(1):61–7.
7. Hannan EL, Kumar D, Racz M, Siu AL, Chassin MR. New York State's cardiac surgery reporting system: four years later. Ann Thorac Surg. 1994;58(6):1852–7.
8. Malenka DJ, O'Connor GT. The Northern New England Cardiovascular Disease Study Group: a regional collaborative effort for continuous quality improvement in cardiovascular disease. Jt Comm J Qual Improv. 1998;24(10):594–600.
9. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg. 1999;16(1):9–13.
10. Fortescue EB, Bates DW, Chertow GM. Predicting acute renal failure after coronary bypass surgery: cross-validation of two risk-stratification algorithms. Kidney Int. 2000;57(6):2594–602.
11. Puskas JD, Kilgo PD, Thourani VH, Lattouf OM, Chen E, Vega JD, Cooper W, Guyton RA, Halkos M. The society of thoracic surgeons 30-day predicted risk of mortality score also predicts long-term survival. Ann Thorac Surg. 2012;93(1):26–33 (**discussion 33–25**).
12. Ad N, Holmes SD, Patel J, Pritchard G, Shuman DJ, Halpin L. Comparison of EuroSCORE II, original EuroSCORE, and the society of thoracic surgeons risk score in cardiac surgery patients. Ann Thorac Surg. 2016;102(2):573–9.
13. Algarni KD, Maganti M, Yau TM. Predictors of low cardiac output syndrome after isolated coronary artery bypass surgery: trends over 20 years. Ann Thorac Surg. 2011;92(5):1678–84.
14. Dhanani J, Mullany DV, Fraser JF. Effect of preoperative renal function on long-term survival after cardiac surgery. J Thorac Cardiovasc Surg. 2013;146(1):90–5.
15. Husain-Syed F, Ricci Z, Brodie D, Vincent JL, Ranieri VM, Slutsky AS, Taccone FS, Gattinoni L, Ronco C. Extracorporeal organ support (ECOS) in critical illness and acute kidney injury: from native to artificial organ crosstalk. Intensive Care Med. 2018;44(9):1447–59.
16. Whitlock RP, Devereaux PJ, Teoh KH, Lamy A, Vincent J, Pogue J, Paparella D, Sessler DI, Karthikeyan G, Villar JC, et al. Methylprednisolone in patients undergoing cardiopulmonary bypass (SIRS): a randomised, double-blind, placebo-controlled trial. Lancet. 2015;386(10000):1243–53.
17. Fujii Y. Evaluation of inflammation caused by cardiopulmonary bypass in a small animal model. Biology (Basel). 2020;9(4):81.
18. Kristensen SD, Knuuti J, Saraste A, Anker S, Bøtker HE, Hert SD, Ford I, Gonzalez-Juanatey JR, Gorenek B, Heyndrickx GR, et al. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J. 2014;35(35):2383–431.
19. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017;38(36):2739–91.
20. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2017;70(2):252–89.
21. Nishimura RA, O'Gara PT, Bavaria JE, Brindis RG, Carroll JD, Kavinsky CJ, Lindman BR, Linderbaum JA, Little SH, Mack MJ, et al. 2019 AATS/ACC/ASE/SCAI/STS expert consensus systems of care document: a proposal to optimize care for patients with valvular heart disease: a joint report of the American Association for Thoracic Surgery, American College of Cardiology, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2019;73(20):2609–35.
22. Massé L, Antonacci M. Low cardiac output syndrome: identification and management. Crit Care Nurs Clin North Am. 2005;17(4):375–83.
23. Rihal CS, Naidu SS, Givertz MM, Szeto WY, Burke JA, Kapur NK, Kern M, Garratt KN, Goldstein JA, Dimas V, et al. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care: endorsed by the American Heart Assocation, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. J Am Coll Cardiol. 2015;65(19):e7–26.
24. Lomivorotov VV, Efremov SM, Kirov MY, Fominskiy EV, Karaskov AM. Low-cardiac-output syndrome after cardiac surgery. J Cardiothorac Vasc Anesth. 2017;31(1):291–308.
25. Hoffman GM, Niebler RA, Scott JP, Bertrandt RA, Wakeham MK, Thompson NE, Ghanayem NS, Stuth EA, Mitchell ME, Woods RK, et al. Interventions associated with treatment of low cardiac output following stage 1 Norwood palliation. Ann Thorac Surg. 2020;111:1620–7.
26. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, Schein RM, Sibbald WJ. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest. 1992;101(6):1644–55.
27. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A: Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. #N/A 2007;11(2):R31.
28. Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2). Eur J Cardiothorac Surg. 2012;42(5):S45-60.
29. Ortega-Loubon C, Fernández-Molina M, Carrascal-Hinojal Y, Fulquet-Carreras E. Cardiac surgery-associated acute kidney injury. Ann Card Anaesth. 2016;19(4):687–98.
30. Bridgewater B. Mortality data in adult cardiac surgery for named surgeons: retrospective examination of prospectively collected data on coronary artery surgery and aortic valve replacement. BMJ. 2005;330(7490):506–10.
31. Sanchez-Pinto LN, Stroup EK, Pendergrast T, Pinto N, Luo Y. Derivation and validation of novel phenotypes of multiple organ dysfunction syndrome in critically ill children. JAMA Netw Open. 2020;3(8):e209271.
32. Ellenberger C, Sologashvili T, Cikirikcioglu M, Verdon G, Diaper J, Cassina T, Licker M. Risk factors of postcardiotomy ventricular dysfunction in

moderate-to-high risk patients undergoing open-heart surgery. Ann Card Anaesth. 2017;20(3):287–96.
33. Maganti MD, Rao V, Borger MA, Ivanov J, David TE. Predictors of low cardiac output syndrome after isolated aortic valve surgery. Circulation. 2005;112(9 Suppl):I448-452.
34. Poullis M, Palmer K, Al-Rawi O, Johnson I, Ridgeway T. Pressure and oxygen debt on bypass—potential quality markers of perfusion? Perfusion. 2012;27(3):244–8.
35. Matteucci M, Ferrarese S, Cantore C, Cappabianca G, Massimi G, Mantovani V, Rossi MB, Beghi C. Hyperlactatemia during cardiopulmonary bypass: risk factors and impact on surgical results with a focus on the long-term outcome. Perfusion. 2020;35(8):756–62.
36. Kunst G, Milojevic M, Boer C, De Somer F, Gudbjartsson T, van den Goor J, Jones TJ, Lomivorotov V, Merkle F, Ranucci M, et al. 2019 EACTS/EACTA/EBCP guidelines on cardiopulmonary bypass in adult cardiac surgery. Br J Anaesth. 2019;123(6):713–57.
37. Puis L, Milojevic M, Boer C, De Somer F, Gudbjartsson T, van den Goor J, Jones TJ, Lomivorotov V, Merkle F, Ranucci M, et al. 2019 EACTS/EACTA/EBCP guidelines on cardiopulmonary bypass in adult cardiac surgery. Interact Cardiovasc Thorac Surg. 2020;30(2):161–202.
38. Licker M, Diaper J, Cartier V, Ellenberger C, Cikirikcioglu M, Kalangos A, Cassina T, Bendjelid K. Clinical review: management of weaning from cardiopulmonary bypass after cardiac surgery. Ann Card Anaesth. 2012;15(3):206–23.
39. Leistner M, Sommer S, Kanofsky P, Leyh R, Sommer SP. Ischemia time impacts on respiratory chain functions and Ca(2+)-handling of cardiac subsarcolemmal mitochondria subjected to ischemia reperfusion injury. J Cardiothorac Surg. 2019;14(1):92.
40. Rodríguez-Cubillo B, Carnero-Alcázar M, Cobiella-Carnicer J, Rodríguez-Moreno A, Alswies A, Velo-Plaza M, Pérez-Camargo D, Sánchez Fructuoso A, Maroto-Castellanos L. Impact of postoperative acute kidney failure in long-term survival after heart valve surgery. Interact Cardiovasc Thorac Surg. 2019;29(1):35–42.
41. Brown JR, Kramer RS, Coca SG, Parikh CR. Duration of acute kidney injury impacts long-term survival after cardiac surgery. Ann Thorac Surg. 2010;90(4):1142–8.
42. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. Clin J Am Soc Nephrol. 2006;1(1):19–32.
43. Zou Z, Zhuang Y, Liu L, Shen B, Xu J, Jiang W, Luo Z, Teng J, Wang C, Ding X. Role of elevated red cell distribution width on acute kidney injury patients after cardiac surgery. BMC Cardiovasc Disord. 2018;18(1):166.
44. Sičaja M, Pehar M, Đerek L, Starčević B, Vuletić V, Romić Ž, Božikov V. Red blood cell distribution width as a prognostic marker of mortality in patients on chronic dialysis: a single center, prospective longitudinal study. Croat Med J. 2013;54(1):25–32.
45. Manolis AS, Tzeis S, Triantafyllou K, Michaelidis J, Pyrros I, Sakellaris N, Kranidis A, Melita H. Erythropoietin in heart failure and other cardiovascular diseases: hematopoietic and pleiotropic effects. Curr Drug Targets Cardiovasc Haematol Disord. 2005;5(5):355–75.
46. Krones E, Pollheimer MJ, Rosenkranz AR, Fickert P. Cholemic nephropathy—historical notes and novel perspectives. Biochim Biophys Acta Mol Basis Dis. 2018;1864(4 Pt B):1356–66.
47. Mandorfer M, Hecking M. The renaissance of cholemic nephropathy: a likely underestimated cause of renal dysfunction in liver disease. Hepatology. 2019;69(5):1858–60.
48. Ramírez M. Multiple organ dysfunction syndrome. Curr Probl Pediatr Adolesc Health Care. 2013;43(10):273–7.
49. Simko LC, Culleiton AL. Cardiogenic shock with resultant multiple organ dysfunction syndrome. Nursing. 2020;50(7):54–60.
50. Zhao X, Gu T, Xiu Z, Shi E, Yu L. Mild hypothermia may offer some improvement to patients with MODS after CPB surgery. Braz J Cardiovasc Surg. 2016;31(3):246–51.
51. Ronco C, Ricci Z, Husain-Syed F. From multiple organ support therapy to extracorporeal organ support in critically ill patients. Blood Purif. 2019;48(2):99–105.
52. Umegaki T, Ikai H, Imanaka Y. The impact of acute organ dysfunction on patients' mortality with severe sepsis. J Anaesthesiol Clin Pharmacol. 2011;27(2):180–4.
53. Cheng Y, Mo S, Wang K, Fan R, Liu Y, Li S, Zhang X, Yin S, Xu Y, Tang B, et al. Mid-term outcome after tricuspid valve replacement. Braz J Cardiovasc Surg. 2020;35(5):644–53.
54. Shiran A, Sagie A. Tricuspid regurgitation in mitral valve disease incidence, prognostic implications, mechanism, and management. J Am Coll Cardiol. 2009;53(5):401–8.
55. Shah AM, Cikes M, Prasad N, Li G, Getchevski S, Claggett B, Rizkala A, Lukashevich I, O'Meara E, Ryan JJ, et al. Echocardiographic features of patients with heart failure and preserved left ventricular ejection fraction. J Am Coll Cardiol. 2019;74(23):2858–73.
56. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010;363(17):1597–607.
57. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, Lockowandt U. EuroSCORE II. Eur J Cardiothorac Surg. 2012;41(4):734–44 (**discussion 744–735**).

Publisher's Note